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The

Journal of Infectious Diseases

FOUNDED BY THE MEMORIAL INSTITUTE FOR INFECTIOUS DISEASES

VOL. 8 *June 15, 1911* No. 4

ETIOLOGY OF CANINE DISTEMPER.*

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HISTORY OF THE DISEASE.

Canine distemper is an acute infectious disease peculiar to dogs. It has been variously termed canine distemper, canine plague, wheel plague, canine glanders, catarrhal fever, etc. It is called by the Germans "Hundestaupe," "Staupe der Hunde," or "Hundekrankheit"; by the French, "maladie des chiens" or "maladie du jeune âge"; and by the Italians "cimurro" or "moccio canino."

Distemper is caused by a specific poison, the etiological factor, probably a micro-organism, which finds its way into the system through the respiratory tract. Young animals are most susceptible to the disease, which is found running its course, according to the textbooks, as a catarrhal fever, affecting at one time or another all the mucous membranes of the body, and often accompanied with certain nervous symptoms and skin eruptions.

As with measles and whooping cough of the human race, very few of the young escape, and, usually, one attack confers immunity. It exists in all countries and may be found at any season of the year, although the spring and summer months are the most favorable

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* Received for publication October 12, 1910.

for its production in the cities. It is said to have been known in the time of Aristotle. Laosson considers that the canine epizootic which raged in Bohemia during the year 1028 was true distemper.

It is the general opinion, however, that it was imported to Europe from America about the middle of the eighteenth century. It was first carried to Spain, whence it rapidly spread to the other European countries. One of the first to write intelligently at any length on the subject was Jenner, who in 1809, while recognizing the true infectious nature of the disease, was the first to differentiate between distemper and rabies, and also the first to show that it was not communicable to man. Later he was disputed by many of the best writers.

D'Youville must have had some conception of its contagious nature, for soon after the middle of the eighteenth century, not long after its introduction into Europe, he caused the rooms and stables where the sick dogs had been housed to be cleansed and disinfected as thoroughly as possible, so that the disease would not be conveyed to other dogs.

Between the years 1818 and 1852 many articles were written concerning the contagious nature of the disease and its communicability to man. Among those who believed that it could be transmitted to man were Waldinger, von Gemmern and Mecke, Delabère-Blain, Funke and Veith. Among those who carried out experiments on dogs to prove it was infectious, and who believed from the results of their experiments that it could not be communicated to man, were Renner and Karle.

The etiology of the disease was early brought into the discussion by Rawitsch, Krause, Zippelius, and Zündel. Chill, catching cold, imperfect nutrition, increased susceptibility and inanition due to lack of sodium salts were some of the most prominent conditions given as the cause.

Whether or not the disease was contagious and the nature of the contagium occupied the minds of most of the observers from this time on. Röll and Hertwig contended that it was not contagious while Transbot, Venuta, Semmer, Trastowo, and Krajewski believed that the disease was brought about by a certain substance or contagium and that this was specific.

Many likened distemper to diseases of man, emphasizing especially the respiratory system and the skin lesion associated with the abdominal symptoms.

Reuter with others contended that equine distemper and canine distemper were of the same etiology, and that the disease could be transmitted from one to the other.

On account of the skin lesion often found in distemper many compared it to cowpox and also to smallpox. Vaccinating, however, with heifer lymph was attended with no success.

For many years the rôle played by the skin lesions was the cause of considerable controversy, Gray, with a small following, contending that the skin lesion could be found in all cases of distemper.

During the past few years many have been actively engaged in attempting to discover the primary cause of the disease, but from the number of different organisms found, and the fact that the results cannot be confirmed, the question of etiology is still an open one, as may be seen from the summary review of this work which now follows.

PREVIOUS STUDIES OF MICROBIOLOGY OF CANINE DISTEMPER.

Semmer (1875) found an exceedingly slender and small bacillus in the blood of affected dogs a few hours after death.

Krajewski (1881) found a micrococcus.

Rabe (1883) found uniform globules of minute size, sometimes lying together in heaps or connected in twos and fours, or in rows of four or five, stained dark blue with methylene violet.

Mathis (1887) found a diplococcus in the fluid of the tissues, sputum, and pustules, which he cultivated in neutral or slightly alkaline broth.

Marcone and Meloni (1888) found cocci similar to staphylococcus.

Jacquot and Legrain (1890) found in pustules motile micrococci.

Millais (1890) found a long bacillus which liquefies gelatin, descending as a flaky mass in the almost clear fluid, which is covered by a whitish scum. Finally, when the whole of the gelatin is liquefied, the flakes gather at the base, and, if stirred, appear to be of a ropy consistency. He also found a micrococcus which he thought was the cause of the lung lesions. The two combined cause the pneumo-distemper.

Schantye (1892) divided distemper into three diseases produced by three distinct organisms.

Jensen (1896) found the pneumonia of distemper to be caused by streptococci.

Valerio (1896) found a bacillus ($0.3 \times 1.2-2.5\ \mu$) on agar plates from mucus of respiratory tract; often dumb-bell shaped; motile; stains by Gram; causes gas bubbles in depth of gelatin stab; does not coagulate milk; clouds broth; isolated from lungs, brain, spinal cord, and pus in frontal sinus.

Babes and Barzanesco (1897) isolated a bacillus in two cases.

Petropawlowsky (1897) found a bacillus similar to the colon bacillus.

Taty and Jacquin (1898) found a diplococcus in the central nervous system which they regarded as the cause of the nervous form of distemper.

Copeman (1900) found a cocco-bacillus in smears from broth, not infrequently in chains, sometimes of considerable length; does not stain by Gram; grows readily on agar at 36° C.; colonies grayish, glistening, semi-translucent; circular, occasionally, and especially at first, the edge is irregular. Grows well in broth, which first is turbid, later a deposit falls, liquid clears somewhat. Slow growth on serum; milk not coagulated; moist, yellowish growth on potato occasionally; gelatin liquefied.

Lignières and Phisalix (1900–1901) found a long bacillus; Gram-negative; non-motile; assumes cocco-bacillary form in guinea-pigs.

Cadiot and Breton (1901) described the infective bronchopneumonia as an independent disease.

Carré (1905) found a filterable virus in the serous discharges. The serous discharges taken at the commencement of the complication are powerfully pathogenic and the virulence is due to an organism small enough to pass through certain filters.

Hewer (1906) found short, small, non-motile bacillus; Gram-negative; fine, white growth on agar; broth slightly clouded with granular sediment and stringy masses; gelatin not liquefied.

PERSONAL OBSERVATIONS—BACILLUS BRONCHICANIS.

Various micro-organisms isolated.—From the beginning of this work, many different organisms were isolated from the sick dogs, especially while my attention was confined to the discharges from the eyes, nose, and contents of the pustules. The conclusion was soon reached, however, from the infrequency and irregularity with which these different organisms were isolated, that they were simply secondary invaders and had nothing to do with the primary infection. As the distemper dog always suffers from one or more of these secondary infections, and since they often cause the most difficult symptoms to contend with, it is rather important to have some idea of them and the conditions under which they are found. It is a fact also, that the majority of investigators have considered these discharges the results of the primary infection and isolated from them the organisms they considered the real cause of the disease. From the results of my postmortem observations, in the dogs experimentally inoculated as well as in other dogs dying from the disease, I believe that the animals succumb to the secondary infections more often than to the primary disease.

The organisms most frequently found are the staphylococci, especially the albus, which are constant in all purulent secondary conditions. In the early stages of the serious eye lesions and in secondary stages of the cough, I have encountered the streptococcus, but not often. When the disease is allowed to run its course, the staphylococcus is often found in the blood, the animal probably dying from the terminal staphylococcus infection.

I have isolated in several instances a small micrococcus, probably the one mentioned by Millais and others. I have endeavored on several occasions to produce symptoms of distemper with this coccus, but have never been able to produce more than an abscess or a swelling at the site of inoculation if injected subcutaneously, while if injected in any other way it never produced symptoms other than a slight rise of temperature.

Several bacilli, resembling morphologically the bacillus I am about to describe more fully, have been isolated from the discharges as well as from the bronchi and lungs, especially in the later stages, but I have never been able to associate them with the primary infection. These are, no doubt, the organisms mentioned by Copeman, Lignières, Phisalix, and others, and from which their vaccines have been made. These organisms grow as a rule rapidly and luxuriantly, some evolving gas with glucose, some liquefying gelatin, while others coagulate milk with the formation of acid, showing that there are several organisms resembling each other morphologically but differing culturally, which may be found associated with the secondary conditions in distemper. With these organisms I have never been able to produce symptoms simulating the true disease. If inoculated subcutaneously they often produce an edematous swelling or an abscess at the site of the inoculation, and even death, and in these cases the organism may be isolated in pure culture from the blood, but that is far from proving that they are the primary cause of the disease.

In the lungs, liver, spleen, blood, etc., from animals dying with severe secondary symptoms, I have often found a large bacillus, which I believe is a terminal invader. Dogs dying when this organism is present always have a putrid, cadaverous odor several days before they die. After death the surrounding atmosphere becomes almost unbearable.

Other organisms have been found from time to time, but not often enough to consider seriously. A few times an anaerobe, resembling somewhat the bacillus of symptomatic anthrax, was isolated from the blood and organs of dogs dying from the disease. Experiments prove that they are not virulent for dogs or other animals.

While working on the eye secretions I isolated from several cases a diphtheroid bacillus resembling the *B. zerosis canis* of Graham Smith. Also, a diphtheroid bacillus was isolated from the lungs of one dog dying from typical symptoms of distemper. These organisms proved to be non-pathogenic for dogs and other animals.

On several occasions at the beginning of this work I attempted to prove the existence of a filterable virus but was never able to confirm Carré's work.

Postmortem examinations.—All autopsies were performed in an aseptic manner, eliminating as far as possible accidental contaminations. The dogs were killed by the injection of 0.5 grain of strychnine into the gluteal muscles. This is a good method, as it causes death in 30 seconds without any struggle.

Routine cultures were taken from the larynx, trachea, large and small bronchi, lungs, and blood. In obtaining cultures from the lungs and smaller bronchi the tissue was placed in a sterile dish, teased, and the juices pressed out. The juices as well as the lung tissue were placed in broth and smeared over the surface of agar.

A bacillus was found that grew slowly and with difficulty when first isolated from the body, so that extreme care was necessary when looking for the colonies. At the end of 24 hours it is often impossible to see anything on the surface of the agar without the use of a lens. The colonies appear as pin points among the larger colonies of other bacteria and at times it is very difficult to isolate the bacillus on account of the overgrowth of other organisms.

The first pure culture of this bacillus was isolated October 23, 1908, and since then 97 strains have been isolated from dogs in all stages of the disease. Two of these cultures were isolated from dogs in the city of New York, showing that the infection is not local in Detroit. I propose to name this bacillus *B. bronchicanis*.

Blood cultures were taken as a routine measure at all autopsies, and at first nothing grew but the organisms of the secondary infections. Later, however, after the bacillus was discovered in the respiratory tract and after it was found to be so difficult to isolate when associated with other organisms on account of its slow growth, the method was changed. The heart was opened aseptically and from 1 to 5 c.c. of blood drawn off with a large pipette and planted in a flask containing 50 c.c. of broth, or distributed in several tubes of broth. After 24 hours in the incubator, plates are made or slant agar inoculated in successive tubes. Such blood cultures were taken in 63 cases. In 29 the cultures were positive, the bacillus being found in 18, in 13 of which it was uncontaminated, in three associated with staphylococcus and in two with unidentified bacteria. The remaining positive blood cultures had staphylococci only in six, staphylococcus with an unknown bacterium in one, and unidentified bacteria in four cases.

CHARACTERISTICS OF BACILLUS BRONCHICANIS.

It is a short, narrow bacillus, usually found single, but often in pairs. In liquid media it may be found at times in long chains or even filaments. In broth culture, grown directly from the dog, the organism may be larger and more oval in form. Does not take the ordinary stains as readily as most bacteria, does not stain by Gram, but stains best with Loeffler's methylene blue, with characteristic bipolar appearance. The organism is actively and progressively motile.

Plain agar stroke.—After 24 hours at 37° C. a moderate growth, filiform and slightly raised; surface moist, glistening, and smooth; growth translucent and of sticky consistency; no odor as a rule. After 72 hours growth tends to spread slightly except near bottom of tube in contact with water of condensation. As growth ages it has a tendency to become slimy, but retains its other characteristics. Stale or musty odor at times.

Plain agar stab.—After 24 hours at 37° C. a filiform growth, better near the surface. Surface growth moderate, raised and restricted; after 48 hours growth retains form with surface spreading slightly; in 7 days surface growth tends to be restricted, although some strains spread gradually; growth is slimy and smooth.

Potato.—After 24 hours at 37° C. growth rather abundant; surface uneven, raised, moist, glistening, and contoured, and of light tan color; consistency, sticky; decided odor of stale bread; medium slightly darkened. After 48 hours growth thicker, with tendency to spread; color darker tan; medium much darker. In 72 hours the surface of medium nearly covered with growth which has become slimy.

Loeffler's blood serum.—After 24 hours at 37° C. growth is scanty, filiform, smooth, moist, glistening, and nearly flat; no color; medium not colored nor liquefied. In 48 hours the growth has increased slightly. After 30 days no special change in growth; medium browned, but not liquefied. Water of condensation decidedly alkaline.

Koch's blood serum.—After 24 hours at 37° C. growth scanty, filiform, smooth, moist, glistening, and slightly raised; of light tan color; musty odor; medium not colored nor liquefied. In 48 hours growth increased slightly but no other change; in 72 hours medium not liquefied; water of condensation decidedly alkaline. After 3 weeks no change.

Gelatin stab.—After 24 hours a filiform growth which is best on top; surface growth restricted; no liquefaction; medium not changed. In 30 days the characteristics remain the same; no liquefaction.

Nutrient broth.—In 24 hours at 37° C. no surface growth; moderate clouding which is persistent; compact sediment which is easily broken up on shaking; odor rather stale. In 72 hours cloudiness increased; sediment rather viscid; odor decidedly stale, which becomes putrefactive at times.

Growth in dextrose, mannite, maltose, saccharose, lactose, and glucose broth, in fermentation tube for seven days at 37° C., leaves fluid in open arm clouded; no visible growth in closed arm; no gas; broth alkaline.

Litmus milk.—After 24 hours at 37° C. no change. In 72 hours upper half-inch of medium has taken a deeper blue color. After 5 days color entirely disappearing from the bottom of the tube ; color at top deeper blue; brownish, slimy sediment in bottom of the tube. In 3 weeks some strains show color to have entirely disappeared from most of the medium.

Milk.—After 24 hours at 37° C. no change; in 72 hours no coagulation, no acid, sediment starting to form in bottom of tube; after 14 days color of medium light tan; slightly translucent and clouded; sediment is thick and slimy; odor stale.

No growth in Uschinsky & Cohn's solutions.

Dunham's solution.—After 7 days at 37° C. fair growth, with sediment in bottom of tube. Test for indol negative.

Colonies on agar.—After 24 hours at 37° C. colonies small, round, sometimes not much larger than a pin point; translucent and slightly raised. In 38 hours about size of a pin head; round, convex, smooth, amorphous and translucent; edge entire. In 72 hours colony has grown larger, but characteristics about the same; edge may have become undulate. After 7 days colony much thicker; grumose in center; edge undulate.

Colonies on gelatin.—Similar to those on agar; medium not liquefied.

EXPERIMENTAL DISTEMPER.

Method of caring for the dogs before and during the experiment.—In order to carry inoculation experiments to a successful termination and be sure that the dogs were not accidentally infected, three large rooms in buildings isolated from each other were used, each room being in charge of a different attendant. The pups used were taken directly from their mother as soon as weaned. After making sure that the pups were in a healthy condition, they were at once given a bath, and then thoroughly soaked in a germicidal solution and placed in the incubation room. Here they were allowed to remain from three to six weeks under strict observation, in the charge of a man who kept away from other dogs. From the incubation room the pups were placed in another room, where they remained under observation at least three weeks longer before experiments were made. The floors and walls of these rooms were of cement, making it possible to wash and spray thoroughly with a germicidal solution as often as deemed necessary. The rooms were thoroughly disinfected and cleaned before the reception of each lot of pups and after each experiment. They were under lock and key and no one was allowed to enter except the attendant, laboratory assistants, and myself. Following these precautions and with careful feeding and handling, one could be reasonably sure that all abnormal symptoms following inoculations were due directly and solely to the treatment. In a third room, in a building far removed from the first two, were kept all convalescing, as well as all sick, dogs and others under observation and treatment. All autopsies were held in the laboratory, where cultures could be taken conveniently without fear of contamination.

A detailed account of this work has been given, because as far as I am able to learn none of the previous experimenters on distemper have mentioned taking any special care during their inoculations and after treatment.

The dogs were inoculated intratracheally or the broth culture was poured into the nostrils. Inoculating subcutaneously or intravenously did not lead to the development of any typical symptoms.

Dog No. 91.—October 28, 1908: Inoculated subcutaneously (strain No. 36).

October 30: Died. Organism seen in blood smears; no growths.

Dog No. 93.—October 31, 1908: Inoculated directly into lungs (strain No. 36). Cough, no discharge from nose or eyes.

December 3: Died. No discharge from nose or eyes. From lungs isolated *B. bronchicanis* and staphylococcus.

Dog No. 94.—November 2, 1908: Inoculated intraperitoneally (strain No. 36 carried through pig No. 13).

November 7: No symptoms.

November 13: Discharge from eyes.

November 14: Died. Discharge from eyes, and emaciation. *B. bronchicanis* not found.

Dog No. 96.—November 7, 1908: Inoculated intrapulmonarily (strain No. 36 carried through pig No. 14).

November 8: Would cry out if thorax was pressed.

November 9: Died. Consolidation of one lung and part of the other. Smears from lungs show diplococcus, large bacillus and short bacillus, which was probably the *B. bronchicanis*, but it was not isolated.

Dog No. 97.—November 7, 1908: Inoculated intrapulmonarily (strain No. 36 carried through pig No. 15).

No symptoms or signs but emaciation.

November 11: Died. Abdomen filled with fluid. Spleen, liver, and gall bladder swollen. Lungs apparently normal. *B. bronchicanis* found in cultures taken from spleen, liver, bile, and blood.

Dog No. 98.—November 11, 1908: Inoculated intraperitoneally (strain No. 96).

November 13: Watery discharge from eyes; very weak.

November 16: Much weaker; emaciation; killed with strychnine.

Cultures from peritoneum and blood gave no growth.

Dog No. 99.—November 11, 1908: Inoculated subcutaneously (strain No. 96).

November 13: Tumor at site of inoculation; watery discharge from eyes; killed with strychnine.

Culture from abscess, eyes, and blood. No growth of *B. bronchicanis.*

Dog No. 103.—February 9, 1909: Inoculated intraperitoneally (strain No. 36 carried through pig No. 16).

February 10: Very quiet, would not eat.

February 11: Found dead. Peritoneum congested and covered with thick stringy exudate.

Cultures from peritoneum, spleen, and blood sterile.

Dog No. 123.—May 19, 1909: Cultures smeared over face and nostrils (strain No. 108).

May 28: Coughing today.

June 12: Inoculated again, into trachea.

June 14: Diarrhea; slight mucous discharge from nostrils.

June 23: Has had slight cough; no discharge from nostrils or eyes; killed with strychnine.

Both lungs edematous and congested; *B. bronchicanis* found in lungs.

Dog No. 125.—May 20, 1909: Inoculated subcutaneously (strain No. 108).

May 29: No symptoms. Placed in cage just vacated by dog No. 126 which had a typical case of distemper.

June 3: Began to cough today.

June 4: Coughing badly; gave first dose of vaccine.

June 8: Vaccinated again.

July 6: Died. Very emaciated; lungs consolidated; necrotic patches in lungs; *B. bronchicanis* and staphylococcus isolated.

Dog No. 126.—May 29, 1909: Smeared over nostrils and eyes (strain No. 109).

May 26: Coughing and looks ill.

May 28: Very sick; cough; discharge from nose and eyes; vomiting.

June 3: Still coughing and sick.

June 30: Marked emaciation; discharge from nose and eyes; found dead. *B. bronchicanis* found uncontaminated in lungs. Blood sterile.

Dog No. 132.—June 3, 1909: Culture poured into nostrils (strain No. 109).

August 4: Apparently no symptoms but emaciation; killed with strychnine; *B. bronchicanis* and few staphylococci found in lungs; pure culture of *B. bronchicanis* in trachea.

Dog No. 133.—June 3, 1909: Culture poured into nose (strain No. 160).

June 9: Discharge from nose; appears very sick.

August 4: Marked emaciation; killed; *B. bronchicanis* and staphylococci found in lungs and trachea.

Dog No. 134.—June 3, 1909: Poured into nose (strain No. 109).

June 9: Discharge from nose; marked skin eruption; pustules.

June 11: Very weak and almost moribund; killed with strychnine; opacity of both corneae; discharge from eyes and nose; skin eruption; pure culture of *B. bronchicanis* found in lungs.

Dog No. 148.—August 17, 1909: Inoculated into trachea (strain No. 160).

August 19: Extremely quiet.

August 21: Slight discharge from nose; sneezes now and then.

August 26: Culture sprayed into nostrils.

August 31: Inoculated again into trachea.

September 16: No more symptoms; put into convalescing room; recovered.

Dog No. 150.—August 17: Inoculated into trachea (strain No. 160).

August 19: Quiet.

August 22: Quiet.

August 26: Sprayed culture into nostrils.

August 30: Coughed today several times; bowels very loose.

August 31: Inoculated again into trachea.

September 16: No other symptoms; recovered.

Dog No. 154.—August 26, 1909: Inoculated into trachea (strain No. 160).

August 27: Quiet.

August 28: Appears ill.

August 30: Vomited.

September 2: Vomited.

September 16: No more symptoms.

October 26: Killed with strychnine; *B. bronchicanis* found uncontaminated in lungs; in blood a larger bacillus was found.

Dog No. 155.—August 12, 1909: Inoculated into trachea (strain No. 160).

August 13: Very quiet.

August 14: Appetite poor.

August 18: Coughing today.

August 20: Still coughing.

August 22: Watery discharge from nose; does not cough much at present.

August 26: Sprayed culture into nostrils.

September 1: Very quiet.

September 16: Loss of flesh; no other sypmtoms; put into convalescing room.

October 23: Killed with strychnine; cultures from lungs show *B. bronchicanis* uncontaminated.

Dog No. 156.—August 12, 1909: Inoculated into trachea (strain No. 160).

August 13: Very quiet.

August 14: Not eating much.

August 18: Diarrhea; cough today.

August 19: Coughing a great deal.

August 22: Watery discharge from nose; does not cough so much.

August 26: Sprayed culture again into nostrils.

September 1: Very quiet.

September 16: Loss of flesh. No other symptoms or signs of distemper.

October 23: Killed with strychnine; *B. bronchicanis* uncontaminated in lungs and trachea.

Dog No. 159.—August 12, 1909: Inoculated into trachea (strain No. 160).

August 13: Very quiet.

August 14: Appetite poor.

August 16: Suspicious cough.

August 17: Much thinner.

August 18: Coughing today.

August 19: Coughing hard.

August 21: Slight discharge from nose; sneezing.

August 22: Purulent discharge from nose.

August 23: Discharge from nose very bad.

August 31: Inoculated again into trachea.

September 1: Very quiet.

September 16: Symptoms improved.

October 27: Killed with strychnine; *B. bronchicanis* uncontaminated in lungs; blood sterile.

Dog No. 163.—September 27, 1909: Inoculated into trachea (strain No. 169).

September 30: Coughing.

October 2: Very sick; coughing a great deal; vomiting; severe diarrhea.

October 3: Continues to be sick; stools watery and foul.

October 7: Still sick and coughing.

October 17: Still coughing. Put into contaminated room.

November 18: Developed a discharge from eyes and nose; very sick past week; died during the night; opacity of both corneae; complete consolidation of both lungs; smears from lungs showed several different organisms; *B. bronchicanis* not isolated.

Dog No. 164.—September 27, 1909: Inoculated into trachea (strain No. 169).

October 5: Coughing today.

October 21: Symptoms remain the same; put into contaminated room.

November 13: Been failing past week or so; discharge from eyes and nose; cough; found dead; lung consolidated in areas; cloudy fluid in peritoneal cavity; *B. bronchicanis* isolated.

Dog No. 166.—September 27, 1909: Inoculated into trachea (strain No. 169).

September 29: Coughing and sick.

September 30: Very sick and coughing.

October 1: Accidently killed; consolidation in areas in both lungs; mucopurulent exudate in trachea; smears from lungs and trachea show enormous numbers of *B. bronchicanis* which is found in pure culture in lungs and trachea and isolated with another bacillus from blood.

Dog No. 167.—September 27, 1909: Inoculated into trachea (strain No. 169).

September 29: Coughing.

October 2: Sick and coughing.

October 5: Slight purulent discharge from both eyes; still coughing.

October 21: Symptoms improved, but still coughing.

October 26: Cough has increased; killed with strychnine; lungs consolidated; cultures from lungs, trachea, and blood; *B. bronchicanis* uncontaminated from lungs and trachea.

Dog No. 184.—November 16, 1909: Inoculated *B. bronchicanis* into trachea (strains Nos. 164 and 191).

November 20: Coughing frequently.

November 21: Very quiet.

November 22: Coughing and very ill; loss of appetite.

November 25: In very bad condition.

November 26: Found dead today; from appearances died in convulsions; *B. bronchicanis* found in lungs and blood.

Dog No. 186.—November 16, 1909: Inoculated *B. bronchicanis* into trachea (strains Nos. 164 and 191).

November 20: Coughing continually.

November 21: Very quiet.

November 22: Very sick dog; appetite poor; abscess at site of inoculation.

November 23: Found dead today; much loss of flesh; *B. bronchicanis* in lungs.

CONCERNING THE PRIMARY INFECTION.

The important symptoms which may be found in typical distemper are cough, diarrhea, vomiting, purulent discharges from the eyes and nose, skin eruptions, and nervous manifestations, as convulsions and muscular twitchings or choreiform movements. The symptoms always looked for, however, are the purulent discharges from the eyes and nose. With the exception of the cough, the other symptoms are not always present.

Many veterinarians and others refuse to call a case distemper without the eye and nose symptoms, and yet, judging from the many cases I have seen from before the onset of the disease and watched till death, I feel positive that these particular symptoms are due to secondary infections and are not true manifestations of the disease. From the fact that in later stages of the disease, cultures taken from the mucous lining of the respiratory tract and also from the heart's blood show so many different organisms, and that the earlier in the disease the cultures are taken the less frequently are these organisms found, it seems to me that we have been diagnosing the disease from its secondary infections and complications. Arguing from this point, one would expect, if going back far enough in the disease, to find the causative agent unaccompanied by any other organism. And I find that in the first few days of the infection, the secondary organisms are not present at all, but *B. bronchicanis* in pure culture. Also, in many of the cases in the later stages, the smaller bronchi contain the bacillus in pure culture. The higher up in the respiratory tract, the greater variety of organisms found. In the early stages I have never failed in finding this organism in pure culture and often as high up as the trachea.

During March, 1909, I collected about 20 young normal pups for experimental purposes. They were raised in our stables and carefully watched from birth, so as to be sure of their age and condition. As they were healthy and normal, they were all allowed to run together in one large room which was kept as clean as possible at all times.

About the first week in the following May a dog with typical distemper came in contact with the keeper of these pups. The disease was carried from the keeper to the pups, which began to show symptoms in a few days.

Considering this a rare opportunity to watch an epidemic in pups of the same age, from the very day of infection strict clinical records were kept, and the pups were killed on succeeding days, starting with the second day, so that cultures were taken at all stages of the disease.

As already mentioned, if the dogs are killed early enough in the disease, *B. bronchicanis* is present in pure culture in every case. This is shown by cases 105, 106, 107, and 108 of the epidemic of May, 1909, just mentioned and also in the dog No. 170, October 5, 1909, and 245, April 17, 1910, and others occurring sporadically. As the dogs 105, 106, 107, and 108 were from an epidemic, no one would question that they had distemper, and yet there was no discharge from the eyes or nose, no skin eruption, but simply a slight cough and convulsions.

Dog No. 245 was killed as soon as possible after the onset of the symptoms, while dog No. 170 died in a convulsion.

Dog No. 105.—May 10, 1908: Convulsions.

May 12: Slight cough.

May 15: Very ill; cough.

May 17: Killed; *B. bronchicanis* found uncontaminated from the upper trachea down.

Dog No. 106.—May 12, 1908: Convulsions; cough.

May 15: Cough increased.

May 18: Killed; *B. bronchicanis* found uncontaminated.

Dog No. 107.—May 12, 1908: Cough.

May 15: Cough increased.

May 16: Diarrhea; skin eruption.

May 18: Killed and autopsied; *B. bronchicanis* found uncontaminated.

Dog No. 108.—May 15, 1908: Cough.

May 17: Cough increased.

May 18: Killed; *B. bronchicanis* found uncontaminated through the entire respiratory tract.

Dog No. 170.—October 6, 1909: Suffering in the morning with convulsions, died in the afternoon in a prolonged convulsion; *B. bronchicanis* found uncontaminated.

Dog No. 245.—April 10, 1910: Symptoms of being ill past few days.

April 14: Prolonged convulsions in the morning; very weak; killed; *B. bronchicanis* found uncontaminated in the respiratory tract and also in the blood.

In all of these cases *B. bronchicanis* was obtained in pure culture from the respiratory tract and also in the blood of dog No. 245. The fact that in dogs Nos. 170 and 245 the culture was uncontaminated and in No. 245 in the blood as well, shows that they were typical cases of distemper taken in the very first stages and similar to Nos. 105, 106, 107, and 108. This is shown also by the fact that the culture from No. 245 injected into a healthy pup, No. 250, produced a typical case of distemper.

Dog No. 250: April 18: Injected.
April 19: Very quiet.
April 20: Coughed once or twice.
April 21: Coughed several times this morning.
April 25: Coughing most of the time; losing flesh.
April 28: Very sick; coughing continually; vomiting.
April 30: Cough; vomiting; diarrhea; no appetite; sneezing.
May 1: Slight watery discharge from nose.
May 3: Purulent discharge just starting from nose; coughing and sneezing constantly; very thin.
April 5: Purulent discharge from nose increasing.
April 7: Slight watery discharge from eyes.
April 10: Began to improve.

Furthermore, the culture from No. 245 has been agglutinated with the serum of every case of distemper tried, while the controls gave no agglutination; and the serum from No. 245 agglutinated every strain of *B. bronchicanis* tried.

The next symptom after the bronchial to make its appearance is the serous discharge from the nose and eyes, usually from the nose first as is illustrated by dog No. 109, killed a few days later in the disease.

Dog No. 109.—May 15: Cough.
May 17: Diarrhea.
May 18: Slight discharge from nose.
May 19: Killed; *B. bronchicanis* pure from bronchi.

The eyes soon become affected, while the discharge from the nose is becoming more and more purulent. First it is mucopurulent, then thick, purulent.

Dog No. 110.—May 15: Cough.
May 17: Diarrhea.
May 19: Slight discharge from nose.
May 21: Slight discharge from eyes, convulsions.
May 23: Purulent discharge from nose and beginning from eyes.
May 24: Died. The cultures here were contaminated with the staphylococcus, showing that the secondary organisms were beginning to invade the field.

Nos. 111, 116, and 117, which were allowed to go on to death, give a typical picture of true distemper.

Dog No. 111.—May 16: Cough.
May 17: Diarrhea.
May 19: Slight discharge from nose.
May 20: Slight discharge from eyes.
May 22: Purulent discharge from nose.
May 24: Purulent discharge from eyes; skin eruption.
June 6: Died.
Dog No. 116.—May 16: Cough.
May 17: Diarrhea.
May 19: Slight discharge from nose.
May 21: Slight discharge from eyes.
May 22: Purulent discharge from nose and eyes.
June 1: Died.
Dog No. 117.—May 16: Cough.
May 18: Diarrhea.
May 19: Slight discharge fron nose.
May 20: Slight discharge from eyes.
May 23: Purulent discharge from eyes and nose.
June 2: Died. Most all of the tubes were contaminated with other organisms, and many were overrun with the staphylococcus, showing that the secondary organisms are the predominating ones at this stage.

In No. 117 the staphylococcus was found in the blood as well as through the whole respiratory tract, and it was with difficulty that *B. bronchicanis* was isolated at all. Just at this stage I believe is where the previous investigators failed. They waited until the discharges made their appearance before taking their culture, and most of them obtained the supposed causative organism from these discharges.

If the diseased dogs do not succumb but are allowed to go on to recovery, the secondary symptoms will entirely disappear, leaving the dog in an apparently normal condition. Now, if the dogs are killed at this stage, and cultures are obtained from their respiratory tract, it will be found that the secondary invaders have also disappeared, but that the primary organisms are still present. These can usually be found in pure culture several weeks after the dogs have completely recovered. This is shown in Nos. 118, 119, and 120.

Again, if the pups which have been experimentally infected with *B. bronchicanis* are kept in clean and disinfected cages, if the fecal discharges are washed away at once and the dogs are bathed in a disinfecting solution, the secondary organisms rarely cause any trouble and the dogs will show symptoms referable only to the primary infection.

On the other hand, if the pups are placed in an unclean room along with other dogs, and allowed to run unchecked in the dirt and feces, they may be attacked with the secondary symptoms which have hitherto not made their appearance and at the same time they may be recovering from the primary infection, or the primary infection may have entirely disappeared. This is illustrated by dogs Nos. 163 and 164.

Dog No. 163.—September 27, 1909: Inoculated.

September 30: Coughing.

October 2: Very sick, coughing severely.

October 3: Stools watery and of foul odor.

September 7: Still very sick and coughing.

September 17: Still coughing. Put into convalescing room.

November 18: Developed a discharge from eyes and nose; very sick; opacity of both corneae; complete consolidation of both lungs; smears from lungs show several different organisms; *B. bronchicanis* not isolated.

Dog No. 164.—September 27: Inoculated.

October 5: Coughing.

October 21: Symptoms have not changed. Put into convalescing room.

November 13: Been failing past week; discharge from eyes and nose; cough; found dead; lung consolidated in areas; cloudy fluid in peritoneal cavity; *B. bronchicanis* isolated.

Nos. 112, 113, and 115 from the epidemic recovered from the disease and were killed, but we were unable to obtain any culture of the *B. bronchicanis* from them. These three pups were among those vaccinated, which recovered. The vaccine may have had something to do with the disappearance of the organism from the respiratory tract.

The question has naturally been raised many times, whether this organism is not a normal habitant of the dog's respiratory tract. Early in the investigation, and also several times since, I have had occasion to kill and autopsy many, apparently normal, dogs, and in only three cases have I found this organism. It was then in pure culture. The dogs in question were some which had been associated with those suffering with the disease, but did not succumb themselves.

As far as I have been able to learn, the trachea and bronchi of healthy dogs are sterile, and it is only when the resistance is lowered or in diseased conditions that bacteria may be found growing in those situations. With this thought in mind, cultures were taken from the larger bronchi of three dogs by means of a bronchoscope. Two of the dogs were healthy and from all appearances perfectly normal; the other dog had been showing symptoms of indisposition for a few days, as loss of appetite, tendency to lie around, etc. After 24 hours all tubes from the normal dogs were sterile, while those from the sick dog showed the staphylococcus, a small micrococcus, and *B. bronchicanis.* Three days after this the sick dog was found dead and cultures from the respiratory tract as well as the blood showed the staphylococcus and *B. bronchicanis.* The lung was completely consolidated, and cultures gave a micrococcus.

It seems clear that the epidemic of May, 1909, was a typical one of distemper, that it was due to *B. bronchicanis* which was isolated in pure culture in the early stages; and that the symptoms considered typical of distemper, as the purulent discharge from the eyes and nose, were due to secondary organisms.

AGGLUTINATION, PROTECTIVE INOCULATION.

Agglutination by serum of dogs with spontaneous distemper.—The emulsions for the agglutination tests were made from 18-hour agar cultures, taken off in physiological salt solution, to which was added enough formaldehyde to make a one per cent solution. This emulsion was allowed to stand five hours at room temperature, which time was sufficient to kill all the organisms. The tubes were placed in the incubator and read at the end of 24 hours. The control animals were in most cases young and healthy dogs. In order to test as many normal dogs as possible, different controls were used for each experiment, and in all 13 dogs were used. All except one gave a negative result. In this case the animal was from the dog pound and it was not possible to learn whether it had ever suffered from distemper. In every experiment, dogs suffering with distemper gave typical agglutinations, ranging from 1 in 40 to 1 in 800. In several cases in which the serum gave positive results, the strains isolated after death gave positive reactions with the serum of other distemper dogs, and in one case an agglutination test with positive results was made with the homologous serum obtained on the day the dog in question died.

Experiment 4.—This experiment was to test the agglutinative power of a serum from a typical case against several strains isolated at different places. Strain No. 36 was the first strain isolated, about two years old. Strains Nos. 199 and 200 were obtained in New York and were about one year old. Strain No. 232 was of recent date, isolated in Detroit.

April 8, 1910: Serum from dog No. 242, black and white, part hound, and very sick with purulent discharges from eyes and nose; severe cough.

	36	199	200	232
1–10..........	+++	+++	+++	+++
1–20..........	+++	+++	+++	+++
1–40..........	+++	+++	+++	+++
1–60..........	+++	+++	+++	+++
1–80..........	+++	+++	+++	+++
1–100.........	+			+
1–200.........				
1–400.........				
1–600.........				
1–800.........				

Experiment 2.—Test of several serums against one strain.

March 24, 1910: Serum from dogs Nos. 233, 240, 241, all obtained from pound. Controls—well dog, well pup. Emulsions were from culture No. 232.

Dog No. 232 was large, shaggy white, with cough, bloody mucous discharges from nose; quiet, but cross and snappy.

Dog No. 233 was a tan mongrel with cough, weakness; purulent discharge from eyes and nose developed later.

Dog No. 240 was black and tan with purulent discharges from eyes and nose; cough and emaciation.

Dog No. 241 was a mongrel with purulent discharge from nose; cough; very weak.

The two controls were normal, one 6 weeks, one a year old, and perfectly well.

	240	241	233	Well Dog	Well Pup
1–10........	+++	+++	+++	–	–
1–20.......	+++	+++	+++	–	–
1–40.......	++	++	+	–	–
1–60.......	++	++	+	–	–
1–80.......	++	++	+	–	–
1–100......	++	+	......	–	–
1–200......	++	+	......	–	–
1–400......	+	+	......	–	–
1–600......	......	+	......	–	–
1–800......	......	+	......	–	–
1–1000.....	......	......	......	–	–

Agglutination by serum of dogs experimentally infected and of immune dogs.—Young pups were immunized against *B. bronchicanis* by two methods, namely live cultures and killed cultures, both being injected intravenously and subcutaneously.

Experiment 1 was made with serum of dog No. 250, which had been experimentally inoculated with the strain from No. 245. The dog contracted a typical case of distemper, and during convalescence the serum agglutinated the bacillus in dilutions of 1 to 200. Normal serum caused no agglutination.

Experiment 2 was made with serum of dogs Nos. 248 and 249, which had been inoculated with the bacillary strain from No. 245: No. 248 intravenously, and No. 249 subcutaneously. The only marked symptom shown by these two dogs was diarrhea. The serum of No. 248 agglutinated in 1 to 600, serum of No. 249 in 1 to 100; normal serum had no effect.

Experiment 3 was made with serum of these same dogs after two had been immunized by several injections: No. 248 intravenously, and No. 249 subcutaneously. The serum of No. 248 now agglutinated in a dilution of 1–1000, serum of No. 249 in 1–200.

Experiment 4 was made with serum of No. 248, and of dogs Nos. 252 and 253; the latter two were immunized by killed cultures injected subcutaneously. The serum of a guinea-pig (No. 160) was also immunized by repeated injections of the killed cultures subcutaneously, followed by live cultures intraperitoneally, and was tested on the bacillary strain from No. 245.

The results follow:

	248	252	253	Pig 160	Control Dog	Control Pig
1–10.........	+++	+++	+++	++	–	–
1–20.........	+++	+++	+++	++	–	–
1–40.........	+++	+++	+++	++	–	–
1–60.........	+++	+++	+++	+	–	–
1–80.........	+++	+++	+++	+	–	–
1–100........	+++	+++	+++	....	–	–
1–200........	+++	+++	+	....	–	–
1–400........	+++	+++	+	....	–	–
1–600........	+++	++	+	....	–	–
1–800........	+++	++	+	....	–	–
1–1000.......	+++	......	......	....	–	–
1–2000.......	+	......	......	....	–	–
1–4000.......	+	......	......	....	–	–

In Experiment 5 the agglutinative effect of the serum of dog No. 248 was tested on several strains. Strain No. 36 is the first one isolated (New York, October, 1908).

SERUM NO. 248. BACILLARY STRAINS.

	245	199	200	168	36	233
1-10.........	+++	+++	+++	+++	+++	+++
1-20.........	+++	+++	+++	+++	+++	+++
1-40.........	+++	+++	+++	+++	+++	+++
1-60.........	+++	+++	+++	+++	+++	+++
1-80.........	+++	+++	+++	+++	+++	+++
1-100........	+++	+++	+++	+++	+++	+++
1-200........	++	+++	+++	++	+++	+++
1-400........	++	+++	+++	++	+++	+++
1-600........	++	+++	+++	++	+++	+++
1-800........	......	+++	++	++	+++	+++
1-1000.......	......	+++	++	++	+	+
1-2000.......	......	......	++	+	+	+
1-4000.......	......	......	......	+	......	+
1-6000.......	......	......	......	......	......	+

We see that the distemper dogs give the same agglutination tests as the dogs experimentally inoculated with *B. bronchicanis* and also those experimentally immunized by repeated injections.

Protective inoculation.—Experiments were made to test the immunizing properties of *B. bronchicanis* against infection after exposure to the true disease. Forty dogs were used in all. Nine were immunized with live cultures and 17 with dead cultures, while 14 were saved as controls. All of these dogs were exposed to at least three dogs suffering with typical symptoms of the disease, including the respiratory, abdominal, and nervous types. Eight of the controls died while all of the immunized dogs remained well.

Experiments have also been attempted to test the curative properties of a vaccine made from emulsion of the dead organism and the results have so far been encouraging.

CONCLUSIONS.

Canine distemper is found, as a result of this research, to be an acute infectious disease primarily of the respiratory tract of the young dog, caused by a micro-organism first described by me,[1] to which I have given the name *B. bronchicanis*.

These assertions are based on the following facts:

When cultures are taken early in the disease *B. bronchicanis* is found in the respiratory tract in every case, and, if taken in the first stage, is found uncontaminated.

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[1] Preliminary report, *Am. Vet. Rev.*, 1910, p. 499.

B. bronchicanis was isolated from 97 dogs at autopsy. In 68 cases it was isolated in pure culture either from the respiratory tract or blood. Of 29 positive blood cultures it was found 18 times, in 13 of which it was unaccompanied by any other organism.

B. bronchicanis was isolated from the only case attempted during life, in the very earliest stage, by means of the bronchoscope.

The serum from cases of distemper in all stages has given positive agglutination with *B. bronchicanis* while the controls were invariably negative.

Koch's law has been fulfilled and cases of typical distemper have been produced by artificial inoculation with pure cultures, the bacillus being again isolated and grown in pure culture, all under conditions which have precluded infection from any other source.

In the above research I was materially aided by Dr. H. K. Miller and Dr. C. G. Rohrer, of the New York Canine Infirmary, wherein a part of the work was carried on, and also by Dr. T. F. Krey, whose large experience was valuable to me in the clinical portion of the work.

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